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of the now pending claims, as amended, is provided in the section entitled "Pending Claims 18-24, as Amended."

Objection to the Specification

The specification has been amended to comply with the recommendations made by the Examiner.

Claim Rejection - Nonstatutory Double Patenting

Applicant relies on the arguments submitted in the Response filed on May 21, 2001. Applicant further requests that the double patenting rejection be held in abeyance until such time as patentable subject matter is found.

Claim Rejections - 35 U.S.C. §112, Second Paragraph

Claims 18 (and dependent claims 19-20), 21 (and dependent claim 22), and 23 (and dependent claim 24) stand rejected under 35 U.S.C. §112, second paragraph as failing to particularly point out and distinctly claim the subject matter of the invention.

Amended claim 18 recites a method for screening for agents which inhibit the activity of a Kir3.0 channel comprising combining at least two different inward rectifier, G-protein activated, mammalian, potassium Kir3.0 polypeptides to form a functional Kir3.0 channel; combining the candidate agent with the Kir3.0 channel under conditions which permit inward K⁺ current; and determining the induced current, wherein a reduction in the induced current in the presence of the candidate agent as compared to a control is indicative that the agent inhibits the activity of a Kir3.0 channel.

Claim 21 recites a method for screening for agents which inhibit the activity of a Kir3.0 channel comprising providing a functional Kir3.0 channel formed by introducing into an expression host cell a nucleic acid encoding a first mammalian Kir3.0 polypeptide and a nucleic acid encoding a second mammalian Kir3.0 polypeptide under conditions that permit expression of the nucleic acid, wherein the first and second mammalian Kir3.0 polypeptides are different from each other, and wherein the mammalian Kir3.0 polypeptides assemble to form a functional Kir3.0 in the expression host cell; combining a candidate agent with a functional Kir3.0 channel under conditions that permit inward K⁺ current; and determining the induced current, wherein a decrease in the induced current in the presence of the agent as compared to a control is indicative that the agent inhibits the activity of a Kir3.0 channel.

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Claim 23 recites a screening assay for identifying materials which inhibit the activity of a Kir3.0 channel, comprising the steps of introducing nucleic acid encoding a Kir3.0 channel formed from at least two different inward rectifier, G-protein activated, mammalian, potassium Kir3.0 polypeptides into an expression system and causing the expression system to express the nucleic acid encoding a Kir3.0 channel; contacting the Kir3.0 channel with one or more candidate channel-inhibiting materials; and selecting candidate material(s) which inhibit the activity relative to a control performed in their absence.

The Examiner points out that the "metes and bounds" of the Kir3.0 channel, as well as the Kir3.1, Kir 3.2, Kir 3.3, and Kir3.4 polypeptides that are recited in claims 18-24, are not clearly described. In particular, the Examiner asserts that it is not clear whether Kir3.0, Kir3.1, Kir3.2, Kir3.3, or Kir3.4 has a known relationship to the potassium channels disclosed in the specification. The Examiner further maintains that it is not evident whether Kir3.0, Kir3.1, Kir3.2, Kir3.3, or Kir3.4 is a specific species with specific amino acid sequence structures from which percent (%) amino acid sequences may be determined.

Applicant respectfully traverses the rejection.

When the scope (*e.g.*, metes and bounds) of the subject matter embraced by the claims is clear and Applicant has not otherwise indicated an intention that the invention be of a different scope, the claims necessarily comply with the requirements of 35 U.S.C. §112 second paragraph. *In re Borkowski*, 422 F.2d 904, 164 USPQ 642 (CCPA 1970). A second paragraph rejection is therefore only appropriate when the scope of the invention sought to be patented cannot be determined from the language of the claims. *In re Wiggins*, 179 USPQ 421 (CCPA 1973).

The scope of Applicant's invention is readily determined from the language of amended claim 18 and claims 19-24. The "Kir3.0" channel recited in amended claim 18 and claims 19-24 is specifically described in the specification (page 5, lines 15-22) as a G-protein regulated subfamily of the family of inward rectifying potassium channel proteins that are characterized by the presence of two transmembrane domains and a pore region homologous to the pore regions of K⁺, Ca²⁺, or Na⁺ voltage-dependent channels. The Kir3.1, Kir3.2, Kir3.3, and Kir3.4 polypeptides recited in claims 19, 20, 22, and 23 are defined in the specification (page 5, line 23) as individual members of the Kir3.0 subfamily. Examples of the Kir3.0 subfamily which are identified as GenBank accession numbers are specifically provided in the specification. Kir 3.1 is described (page 6, lines 1-3) as comprising *Rattus norvegicus* G-protein-coupled muscarinic potassium channel (nucleotides 1-1827; L25264);

Rattus norvegicus G-protein activated K⁺ channel (nucleotides 1-2070; U01071); *Rattus norvegicus* G-protein activated K⁺ channel, subtype1 (nucleotides 1-2111; U01141); or mouse G-protein coupled inward rectifying potassium channel 1 (nucleotides 1-1679; D45022). Moreover, Kir3.2 is described in the specification (page 6, line 5) as comprising human G-protein coupled inward rectifier potassium channel 2 (nucleotides 1-2074; U24660) and Kir3.3 is described in the specification (page 6, line 7) as comprising *Mus musculus* (mouse) G-protein coupled inward rectifier K⁺ channel 3 (nucleotides 1-2267; U11860). Finally Kir3.4 is described in the specification (page 6, lines 7-9) as comprising *Rattus norvegicus* cardiac KATP (nucleotides 1-1260; X83584), *Rattus norvegicus* potassium channel (nucleotides 1-3156; L35771), *Homo sapiens* cardiac KATP (nucleotides 1-1260; X83582), or *Homo sapiens* G protein-activated inwardly rectifying K⁺ channel (nucleotides 1-1349; L47208). The specification further provides (page 6, lines 18-19) that Kir3.0 multimeric channels vary in their response to G-protein activation based on the specific combinations of Kir3.0 (e.g., Kir3.1, Kir3.2, Kir3.3, or Kir3.4) polypeptides when expressed in *Xenopus laevis* oocytes. For example (page 7, lines 13-18), Kir3.1/Kir3.2 and Kir3.1/Kir3.3 polypeptide combinations show significant enhancement of G-protein induced currents, although Kir3.2/Kir3.3 polypeptide combinations exhibit a decreased G-protein induced current.

In addition, the term "Kir3.0 polypeptide" is defined (page 7, lines 19-21) as a single polypeptide capable of associating with other Kir3.0 polypeptides for forming functional Kir3.0 channels which comprise (page 6, lines 26-28; page 7, line 1) functional multimeric proteins that consist of one or more Kir3.0 (e.g., Kir3.1, Kir3.2, Kir3.3, or Kir3.4) polypeptides from the same or different species. The specification additionally provides that "Kir3.0 channels" (page 7, lines 1-8) are inwardly rectified (e.g., conduct inward but not outward K⁺ current), are blocked by low concentrations of extracellular Cs⁺ or Ba²⁺, and exhibit conductance which is G-protein modulated and dependent on both voltage and E-E_K (e.g., equilibrium potential). Moreover, the GenBank accession numbers recited in the specification for Kir3.1, Kir3.2, Kir3.3, and Kir3.4 provide nucleotide sequences, as well as amino acid sequences, from which number percentages can be calculated. For the foregoing reasons, the 35 U.S.C. §112, second paragraph rejection of amended claim 18 (and dependent claims 19-20), claims 21 (and dependent claim 22), and 23 (and dependent claim 24) stand rejected under 35 U.S.C. §112, second paragraph should be withdrawn.

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Claim Rejections - 35 U.S.C. §112, First Paragraph

Claims 18 (and dependent claims 19-20), 21 (and dependent claim 22), and 23 (and dependent claim 24) stand rejected under 35 U.S.C. §112, first paragraph as not being described in the specification so as to convey that Applicant has possession of the claimed invention. In particular, the Examiner asserts that the function and structure of Kir3.0, Kir3.1, Kir3.2, Kir3.3, and Kir3.4 are not adequately described by Applicant. The Examiner further cites *University of California v. Eli Lilly and Co.* 43 USPQ2d 1398 for the proposition that a specification reciting only a description of rat insulin cDNA fails to provide a sufficient written description, under 35 U.S.C. §112 first paragraph, for claims which teach broad classes of vertebrate and mammalian insulin cDNA.

Applicant respectfully traverses the rejection.

Applicant notes that the Examiner has the initial burden of presenting the evidence or reasons establishing why the skilled artisan would not recognize a description of the invention defined by the claims in Applicant's disclosure. *In re Wertheim*, 541 F.2d 257, 265, 191 USPQ 90, 98 (CCPA 1976); *Ex parte Sorenson*, 3 USPQ2d 1462, 1463 (Bd. Pat. App. & Inter. 1987). Applicant maintains that the Examiner has not met this burden and directs the Examiner's attention to MPEP II.A (8th Edition, August 2001) §2163 stating:

There is a strong presumption that an adequate written description of the claimed invention is present in the specification as filed. *In re Wertheim*, 541 F.2d 257, 263, 191 USPQ 90, 97 (CCPA 1976)....Consequently, rejection of an original claim for lack of written description should be rare. MPEP § 2163 (II.A).

Applicant notes that the structure and function of Kir3.0 (*e.g.*, comprised of individual members Kir3.1, Kir3.2, Kir3.3, and Kir3.4) is adequately identified and described in the claims, as well as in the specification. The specification recites 11 representative GenBank accession numbers for Kir3.1, Kir3.2, Kir3.3, and Kir3.4, rat, mouse, and human nucleotide sequences, as well as amino acid sequences, that are descriptive of the Kir3.0 channels recited in the claims. Moreover, the examples provide methods for isolating cDNA encoding Kir3.1 using the total RNA extracted from atria and ventricles of 19-21 day-old rats (page 20, line 27-28) as well as methods for isolating cDNA encoding Kir3.2 and Kir3.3 using mouse brain

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RNA (page 29, line 3). Methods are additionally described for the coexpression of Kir3.1/Kir3.2 mRNAs (page 30, lines 1-2) in oocytes for forming heteromultimeric Kir3.0 channels. In addition, the unique properties of the functional multimeric Kir3.0 channels are demonstrated (page 27, lines 7-9; 24-25) in *Xenopus laevis* oocytes which are injected with atrial mRNAs (and mRNAs encoding serotonin receptor) wherein multimeric Kir3.0 channels are formed and inward rectifiers are opened by serotonin that is mediated by G-protein (e.g., $G\beta_{1\gamma_2}$) activation. These multimeric Kir3.0 channels are further expressly demonstrated to exhibit the unique properties of conducting inward but not outward K^+ current, of exhibiting blockage by low concentrations of Ba^{2+} , and of exhibiting channel conductance that is dependent on voltage as well as $(E-E_K)$ (page 27, lines 8-12).

The specification further demonstrates that coexpression of Kir3.2/Kir3.1 in *Xenopus laevis* oocytes produces large G-protein mediated inward currents relative to the individual expression of either Kir3.2 or Kir3.1 (page 31, lines 2-9). The specification additionally describes that coexpression of Kir3.3/Kir3.1 in *Xenopus laevis* oocytes produces large inward currents relative to the expression of Kir3.3 alone (page 33, lines 14-24). Moreover, coexpression of Kir3.3 and Kir3.2 in *Xenopus laevis* oocytes produces small inward currents relative to the expression of Kir3.2 alone (page 33, lines 25-28). For the foregoing reasons, the function and structure of the functional Kir3.0 (e.g., Kir3.1, Kir3.2, Kir3.3, Kir3.4) heteromultimeric channels recited in Applicant's claims are more than sufficiently described in the specification, as well as in the claims. Accordingly, the 35 U.S.C. § 112, first paragraph rejection of amended claim 18 (and dependent claims 19-20), claim 21 (and dependent claim 22), and 23 (and dependent claim 24) should be withdrawn.

Rejection Under 35 U.S.C. § 102(b) - *Yatani, et al.* with evidence from *Krapivinsky, et al.*

Claims 18 (and dependent claims 19-20), 21 (and dependent claim 22), and 23 (and dependent claim 24) are rejected under 35 U.S.C. § 102(b) as being anticipated by *Yatani* with evidence from *Krapivinsky*.

Applicant respectfully traverses.

Applicant relies on the arguments submitted in the Response filed on May 21, 2001. Applicant further notes that rejections under 35 U.S.C. § 102(b) dictate that the claimed subject matter be identically disclosed or described in the prior art. Thus, anticipation under

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35 U.S.C. § 102(b) requires that all of the material elements recited in a claim be found in a single prior art source. In re Marshall (CCPA 1978) 577 F2d 301, 198 USPQ 344. The law is well established that in order to anticipate a claim, the prior art must disclose "each and every element" of the claimed invention. SSIH Equipment S.A. v. U.S. Inc. Int'l. Trade Commission, 218 USPQ 678, 688 (Fed. Cir. 1983). As stated by the Federal Circuit in In re Bond, 15 USPQ2d 1566, 1567 (Fed. Cir. 1990), "[f]or a prior art reference to anticipate in terms of 35 U.S.C. § 102, every element of the claimed invention must be identically shown in a single reference." (Emphasis added). See also Glaverbel Societe Anonyme v. Northlake Marketing & Supply, Inc., 33 USPQ2d 1496 (Fed. Cir. 1995). The prior art cited by the Examiner does not disclose "each and every element" of the claimed invention, and accordingly, *Yatani* (with evidence from *Krapivinsky*) does not anticipate amended claim 18 or claims 21 or 23, under 35 U.S.C. § 102(b).

Yatani discloses guinea pig atrial cells containing endogenous muscarinic potassium channels that are directly activated by G protein (pages 207-208) and inhibited by NAD⁺ (nicotinamide adenine dinucleotide) and PTX (pertussis toxin) (page 209). Applicant's amended claim 18, in contrast, teaches combining at least two different inward rectifier, G-protein activated, mammalian, potassium Kir3.0 polypeptides to form a functional Kir3.0 channel (e.g., multimeric combination of Kir3.1, Kir3.2, Kir3.3, and Kir3.4). *Yatani*, accordingly, fails to teach or disclose combining different Kir3.0 polypeptides to form Kir3.0 channels.

Claim 21, unlike *Yatani*, teaches introduction of nucleic acid into an expression cell, conditions which permit expression of nucleic acids which encode a first and second different Kir3.0 polypeptide, and assembly of the first and second different Kir3.0 polypeptides for forming functional Kir3.0 channels. Applicant notes that *Yatani* fails to teach (1) introduction of nucleic acid into expression cells, (2) conditions which permit expression of nucleic acid, (3) nucleic acid encoding different Kir3.0 polypeptides, (4) Kir3.0 polypeptide assembly, or (5) functional Kir3.0 channels. Accordingly, *Yatani* does not teach or disclose the limitations of claim 21.

Finally, claim 23, unlike *Yatani*, teaches introduction of nucleic acid into an expression system, inducement ("causing") of the expression system to encode nucleic acid, and nucleic acid encoding at least two different Kir3.0 polypeptides. Again, *Yatani* fails to

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teach introduction of nucleic acid into an expression system, inducement of an expression system, or nucleic acid encoding different Kir 3.0 polypeptides. Accordingly, *Yatani* does not teach or disclose the limitations of claim 23. The *Yatani* reference merely discloses potassium channels which are endogenous to guinea pig atrial cells. The *Yatani* reference therefore fails to teach all of the material elements recited in each of claims 21 and 23 and amended claim 18. Applicant therefore respectfully requests that the 35 U.S.C. § 102(b) rejection of amended claim 18 (and dependent claims 19-20) and claims 21 (and dependent claim 22), and 23 (and dependent claim 24) be withdrawn.

The Examiner cites *Krapivinsky* as evidence that cardiac K^+ channels are comprised of heteromultimers. Applicant points out that for a prior art reference to anticipate in terms of 35 U.S.C. § 102, every element of the claimed invention must be identically shown in a single reference." *Glaverbel Societe Anonyme v. Northlake Marketing & Supply, Inc.*, 33 USPQ2d 1496 (Fed. Cir. 1995). Applicant has previously demonstrated that *Yatani* fails to teach every element recited in each of claims 21, 23, and amended claim 18. Because the Examiner has not demonstrated that *Krapivinsky* corrects the deficiencies of *Yatani*, Applicant respectfully requests that the 35 U.S.C. § 102(b) rejection of amended claim 18 (and dependent claims 19-20) and claim 21 (and dependent claim 22), and 23 (and dependent claim 24) be withdrawn.

Rejection Under 35 U.S.C. § 102(b) - *Karschin et al.* with evidence from *Krapivinsky et al.*

Claim 18 (and dependent claims 19-20) are rejected under 35 U.S.C. § 102(b) as being anticipated by *Karschin* with evidence from *Krapivinsky*.

Applicant respectfully traverses.

Applicant relies on the arguments submitted in the Response filed on May 21, 2001. In addition, Applicant notes that *Karschin* only discloses heterologously expressed serotonin receptors which are activated by serotonin and acetylcholine in rat atrial (cardiac) myocytes containing endogenous K^+ channels. Although *Karschin* may disclose that recombinantly expressed serotonin receptors couple to native K^+ channels (*e.g.*, via a G-protein interaction) that are endogenous to rat atrial myocytes, nothing in the reference teaches or discloses

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combining at least two different inward rectifier, G-protein activated mammalian, potassium Kir3.0 polypeptides to form functional Kir3.0 channels, much less the combining of an agent with a Kir 3.0 channel for reducing Kir3.0 channel activity, as required by claim 18.

Karschin merely discloses the types of K^+ channels which are endogenously present in rat atrial myocytes. Because *Karschin* fails to teach every element recited in amended claim 18 and the Examiner has not demonstrated that *Krapivinsky* is able to correct the deficiencies of *Karschin*, Applicant respectfully requests that the 35 U.S.C. § 102(b) rejection of amended claim 18 (and dependent claims 19-20) be withdrawn.

Rejection Under 35 U.S.C. § 102(a) - Duprat, et al.

Claims 18 (and dependent claims 19-20), 21 (and dependent claim 22), and 23 (and dependent claim 24) are rejected under 35 U.S.C. § 102(a) as being anticipated by *Duprat et al.* In particular, the Examiner asserts that *Duprat et al.* discloses the inhibition of inward rectifier currents in various K^+ channels due to the presence of ATP and/or Mg^{2+} .

Applicant respectfully traverses.

Applicant relies on the arguments submitted in the Response filed on May 21, 2001. Applicant additionally points out that ATP and Mg^{2+} factors are necessary for the activity of the channels disclosed in *Duprat et al.* Removal of either ATP or Mg^{2+} from the channels results in a decrease in channel activity (page 660-661) while inclusion of these factors restores channel activity (pages 660- 661). As distinguished from *Duprat*, Applicant's amended claim 18 and claim 21 teach functional Kir3.0 channels, rather than channels without components which are associated with channel activity (*see* abstract, lines 10-12 and page 661, lines 662, lines 1-2; page 660, line 15 and page 661, lines 1-2). Moreover, Applicant's claims require combining (amended claim 18, claim 21) or contacting (claim 23) Kir3.0 channels with candidate inhibitory agents or channel-inhibiting materials in which the presence of the inhibiting agent or material causes a reduction, decrease, or inhibition of the Kir3.0 channel activity. *Duprat* in contrast, discloses the absence, rather than the presence of ATP (or Mg^{2+}) for reducing, inhibiting or decreasing the activity of the channel. In summary, as distinguished from the channels disclosed in *Duprat*, Applicant's channels are functional (*e.g.*, permit inward K^+ current) in the absence of a candidate agent and, moreover, require the

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inclusion of a candidate agent or channel-inhibiting material for reduction or inhibition of inward K^+ current.

Accordingly, Applicant respectfully requests withdrawal of the 35 U.S.C. § 102(a) rejection of amended claim 18 (and dependent claims 19-20), 21 (and dependent claim 22), and 23 (and dependent claim 24).

Applicant submits that the claims are in form for allowance and early notice of such is requested. If the Examiner believes that there are remaining issues which may be resolved by telephone, he is urged to call the undersigned at (415) 781-1989.

Respectfully submitted,

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Date: August 12, 2002



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VERSIONS WITH MARKINGS TO SHOW CHANGES MADE

In the Specification:

The paragraph beginning at page 4, lines 9-15, has been amended as follows:

– Figures 1A-C show inward currents evoked by high K^+ , 5HT and ACh in RNA-injected oocytes. (A) I_{hk} and I_{5HT} in an oocyte injected with atrial RNA + 5HT1A-R RNA. Holding potential in this and all following figures was -80mV. (B) Inward currents evoked by ACh (AcChO) and 5HT in a single oocyte in hK solution. (C) The dependence of I_{5HT} amplitude on 5HT concentration in oocytes of one frog. In each oocyte, the response to one 5HT concentration was tested. Data represent mean \pm SEM in 4-6 cells at each concentration.–

The paragraph beginning at page 4, lines 16-26, has been amended as follows:

– Figures 2A-D depict that I_{hk} and I_{5HT} are inwardly rectifying K^+ currents. (A) Currents evoked by voltage steps from the holding potential of -80 mV to voltages between -140 and 40 mV in 20 mV steps in ND96(a), hK (b), hK in the presence of 5HT (c). Net I_{5HT} (d) was obtained by digital subtraction of (b) from (c). (B) Current-voltage relations of the total membrane current in a representative oocyte in NG 96 (2 mM $[K_{out}]$; \square), in 25 mM $[K^+_{out}]$ \blacklozenge ; in 75 mM $[K_{out}]$ \circ , and in hK (96 mM $[K_{out}]$; \blacktriangle). (C) Current-voltage relation of the net I_{5HT} in the same oocyte as in (B) in 25 mM $[K_{out}]$ \blacklozenge ; 75 mM $[K_{out}]$ \circ , and 96 mM $[K_{out}]$ \blacktriangle . (D) The dependence of the reversal potentials of total membrane current \blacktriangle and of I_{5HT} \bullet on $[K_{out}]$. The straight lines represent least square fits to data (mean \pm SEM, n=3 for each point).–

The paragraph beginning at page 4, lines 27-28, has been amended as follows:

– Figures 3A-D depict the Ba^{2+} block of I_{hk} and I_{5HT} . (A-C) show records taken from the same oocyte at 10 min intervals. Between the records, the cell was bathed in ND96. 5HT concentration was 4 nM. Note that in (B) 300 μ M Ba^{2+} reduces I_{hk} and almost completely blocks I_{5HT} . Ba^{2+} and 5HT were washed out simultaneously, and this resulted in an inward current "tail". (D) dose dependence of BA^{2+} inhibition of I_{hk} in native oocytes \circ , I_{hk} in RNA-injected oocytes \bullet , I_{5HT} in RNA-injected oocytes ∇ . Data are mean \pm SEM, n=3 to 7 for each point.–

The paragraph beginning at page 5, lines 7-13, has been amended as follows:

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– Figures 4A-B depict that I_{5HT} is mediated by activation of a G-protein. (A) The effect of PTX treatment (500 ng/ml, 20-26 h) on I_{hK} and I_{5HT} . The cells were injected with 120 ng/oocyte total atrial RNA, 11 ng/oocyte 5HT1A-R RNA, and, where indicated, with 11 ng/oocyte $G_{12\alpha}$ RNA. (B) GDP- β -S injection inhibits I_{5HT} but not I_{hK} in an oocyte injected with atrial + 5HT1A-R RNAs. 5HT concentration was 0.4 μ M. A small outward current deflection (denoted by ★) upon washout of 5HT was caused by an inadvertent perfusion of ND96 for a few seconds.–

In the Claims:

18. (Amended) A method for screening for agents that inhibit the activity of a Kir3.0 channel, the method comprising:

a) combining [forming a functional Kir3.0 channel from] at least two different inward rectifier, G-protein activated, mammalian, potassium Kir3.0 polypeptides to form a functional Kir3.0 channel;

b) combining the candidate agent with said Kir3.0 channel under conditions that permit inward K⁺ current;

c) determining the induced current, wherein a reduction in said induced current in the presence of said agent as compared to a control is indicative that said agent inhibits the activity of a Kir3.0 channel.

Pending Claims 18-24, as Amended

18. (Amended) A method for screening for agents that inhibit the activity of a Kir3.0 channel, the method comprising:

- a) combining at least two different inward rectifier, G-protein activated, mammalian, potassium Kir3.0 polypeptides to form a functional Kir3.0 channel;
- b) combining the candidate agent with said Kir3.0 channel under conditions that permit inward K⁺ current;
- c) determining the induced current, wherein a reduction in said induced current in the presence of said agent as compared to a control is indicative that said agent inhibits the activity of a Kir3.0 channel.

19. The method of Claim 18, wherein said Kir3.0 polypeptides are selected from the group consisting of polypeptides having at least about 50% amino acid sequence identity with Kir3.1, Kir3.2, Kir3.3 or Kir3.4.

20. The method of Claim 18, wherein said Kir3.0 polypeptides are selected from the group consisting of polypeptides encoded by nucleic acids that hybridize under low stringency conditions with a complement of a nucleic acid which encodes Kir3.1, Kir3.2, Kir3.3 or Kir3.4.

21. A method for screening for agents that inhibit the activity of a Kir3.0 channel, the method comprising:

- a) providing a functional Kir3.0 channel formed by introducing into an expression host cell a nucleic acid encoding a first mammalian Kir3.0 polypeptide and a nucleic acid encoding a second mammalian Kir3.0 polypeptide under conditions that permit expression of said nucleic acid, wherein said first and second mammalian Kir3.0 polypeptides are different from each other, wherein said mammalian Kir3.0 polypeptides assemble to form a functional Kir3.0 in said expression host cell;
- b) combining a candidate agent with a functional Kir3.0 channel under conditions that permit inward K⁺ current;
- c) determining the induced current, wherein a decrease in said induced current in the presence of said agent as compared to a control is indicative that said agent inhibits the activity of a Kir3.0 channel.

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22. The method of Claim 21, wherein said nucleic acid encoding said mammalian Kir3.0 polypeptides are selected from the group consisting of nucleic acids that hybridize under low stringency conditions with a complement of a nucleic acid which encodes Kir3.1, Kir3.2, Kir3.3 or Kir3.4.

23. A screening assay for identifying materials which inhibit the activity of a Kir3.0 channel, comprising the steps of:

(a) introducing nucleic acid encoding a Kir3.0 channel formed from at least two different inward rectifier, G-protein activated, mammalian, potassium Kir3.0 polypeptides into an expression system and causing the expression system to express said nucleic acid encoding a Kir3.0 channel;

(b) contacting the Kir3.0 channel with one or more candidate channel-inhibiting materials;

(c) selecting candidate material(s) which inhibit said activity relative to a control performed in their absence.

24. The method of Claim 23, wherein said nucleic acid encoding a Kir3.0 channel consists essentially of nucleic acids that hybridize under low stringency conditions with a complement of a nucleic acid which encodes Kir3.1, Kir3.2, Kir3.3 or Kir3.4.